

Retraction

by John Newport

A Role for Ran-GTP and Crm1 in Blocking Re-Replication

This paper (Cell 113, 115–125, April 4, 2003) reports results of experiments that together strongly support the conclusion that, in metazoan cells, formation of a complex consisting of the GTP binding protein Ran, the exportin Crm1, and the DNA helicase MCM plays a critical role in limiting DNA replication to a single round each cell cycle. This conclusion is largely based on two experimental results: (1) Experiments which show that a Ran mutant, RanQ69L, that binds GTP but cannot hydrolyze it inhibits incorporation of the MCM helicase into pre-replication complexes (pre-RC's) in *Xenopus* egg extracts. (2) Equally important is the observation that addition of a Ran mutant that cannot bind GTP, Ran T24N, induces both re-binding of MCM helicase to DNA following a single round of DNA replication and induces a second round of replication. Together these results suggested that sequestration of MCM into a Crm1-Ran complex within nuclei during S phase of the cell cycle functioned to limit replication to a single round. In the course of pursuing this model further, a postdoctoral fellow in my laboratory, Dr. Peter Trabold, was able to reproduce results reported using the RanQ69L mutant. However, he was unable to reproducibly observe either the substantial reloading of MCM onto DNA or the robust re-replication reported to occur following addition of Ran T24N. Occasionally, modest excess replication was observed following addition of RanT24N. However, further investigation demonstrated that this replication was most likely due to the transient permeabilization of nuclei caused by addition of RanT24N. Therefore, although experiments using RanQ69L support a model involving the Crm1-MCM complex to limit re-replication, the inability of RanT24N to induce re-replication leaves the model unproven. In light of these new results, I am withdrawing the paper and the conclusions included in it.

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The first author of this article, Ryuji Yamaguchi, is not a coauthor on this retraction because he stands firmly by the data presented in the article.